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عنوان:

بررسی اثر محافظت‌کننده کافئیک اسید و کوئرستین بر آپوپتوز ناشی از محرومیت سرم در سلول‌های بنیادی مزانشیمی مشتق از مغز استخوان

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Title:

Investigation of the protective effect of caffeic acid and quercetin on serum deprivation-induced apoptosis in bone marrow-derived mesenchymal stem cells

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اظهارنامه

اینجانب: مرضیه حیدریان ..... با شماره دانشجویی: 93132310۴1 ..... متعهد می‌شوم موارد مذکور در این پایان‌نامه تحت عنوان:

بررسی اثر محافظت کنندگی کافئیک اسید و کوئرستین بر آپوپتوز ناشی از عصاره سرم رسوبی حاصل از بافت مغز مشتق از مغز استخوان

به راهنمایی: سرکار خانم دکتر/جناب آقای دکتر میرا امیرباقی ..... حاصل فعالیت‌های پژوهشی خود بوده و زیر نظر استادان (راهنما، همکار و مشاور) تهیه شده است و مسئولیت صحت داده‌ها و اطلاعات گزارش شده در این پایان‌نامه را به عهده می‌گیرم. کلیه مطالبی که از منابع دیگر در این پایان‌نامه مورد استفاده قرار گرفته، با ذکر مرجع مشخص شده است.

تمامی حقوق مادی و معنوی این پایان‌نامه (شامل فرمول‌ها، توابع کتابخانه‌ای، نرم‌افزارها، سخت‌افزارها و مواردی که قابلیت ثبت اختراع دارد) متعلق به دانشگاه علوم پزشکی و خدمات بهداشتی درمانی کرمان بوده و هرگونه استفاده تنها با کسب اجازه ممکن خواهد بود. همچنین کلیه حقوق مربوط به چاپ، تکثیر، نسخه برداری، ترجمه، اقتباس و نظائر آن در محیط های مختلف اعم از الکترونیکی، مجازی یا فیزیکی برای دانشگاه علوم پزشکی و خدمات بهداشتی درمانی کرمان محفوظ می باشد. استناد به مطالب و نتایج این پایان‌نامه درصورتی‌که به نحو مناسبی ارجاع داده شود، بلامانع است.

بدینوسیله تایید می‌گردد که نظرات داوران در جلسه دفاع طبق صلاحدید استاد راهنمای اول در متن پایان‌نامه اعمال گردیده است.

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خلاصه

مقدمه: امروزه، سلول‌های بنیادی مزانشیمی (MSC) منبعی امیدوارکننده برای سلول درمـانی در نظـر گرفته شده‌اند. بااین‌حال، برخی از چالش‌ها مانند: کمبود اکسیژن، فقر موادغذایی، وجود رادیکال‌هـای آزاد اکسیژن، افزایش سیتوکین‌های التهابی و سایر عوامل ممکـن اسـت اثربخشـی سـلول درمـانی را کاهش دهند. همه‌ی این دلایل باعث مرگ زودرس سلول‌ها در روزهای اولیه پس از پیوند می‌شـوند. استراتژی‌های مختلفی برای افزایش اثربخشی درمان ارائه شده است. در سال‌های اخیر، توجه زیـادی به استراتژی‌های پیش‌درمانی شده است که تأثیرات بسیار مفیدی در محافظت از سـلول دارد. در ایـن مطالعه، از کافئیک اسید و کوئرستین به‌عنوان دو آنتی‌اکسیدان طبیعی قوی برای محافظت از سلول‌های بنیادی مزانشیمی در برابر آپوپتوز ناشی از محرومیت از سرم استفاده شده است.

روش‌ها: سلول‌های بنیادی مزانشیمی از رت جدا شده، کشت داده شدند، سپس بـا کافئیـک اسـید و کوئرستین با غلظت‌های مختلف در زمان‌های مختلف تحت درمان قرار گرفتند. سپس آن‌ها به مـدت ٤٨ ساعت در معرض شرایط محرومیت سرم قرار گرفتند. پس از آن، بقای سلول با اسـتفاده از روش MTT و آپوپتوز بر اساس بیان پروتئین‌های آپوپتوتیک و آنتی‌آپوپتوتیـک از جملـه Bax و Bcl-2 بـا استفاده از وسترن بلات ارزیابی شد.

نتایج: نتایج مطالعه حاضر نشان داد که پیش درمانی سلول‌های بنیادی مزانشیمی بـا کافئیـک اسـید و کوئرستین پس از ۷۲ ساعت به‌طور قابل‌توجهی باعث افزایش بقای سلول‌ها در شرایط SD می‌شـود. علاوه بر این، وسترن بلات نشان داد که هر دو روش درمانی می‌توانند سطح پروتئین Bax را کـاهش دهند و بیان پروتئین Bcl-2 را در سلول‌های آپوپتوتیک ناشی از SD افزایش دهند.

نتیجه‌گیری: می‌توان نتیجه گرفت که کافئیک اسید و کوئرستین ممکن است به‌عنوان ابزاری امیدوارکننده برای بهبود کارایی سلول درمانی قبل از پیوند استفاده شوند.

کلمات کلیدی: کافئیک اسید، کوئرستین، سلول‌های بنیادی مشتق شده از مغز استخوان، آپوپتوز.

Abstract

Introduction: Nowadays, mesenchymal stem cells (MSCs) are considered a promising source for cell therapy. However, some challenges such as lack of oxygen, nutritional deficiency, the presence of oxygen free radicals, increased inflammatory cytokines and other factors may reduce the effectiveness of cell therapy**.** All of which cause premature death of these cells in the early days after transplantation Different strategies have been proposed to increase the effectiveness of treatment. In the recent years, much attention has been paid to preconditioning strategies, which has very beneficial effects on cellular protection. In this study, caffeic acid and quercetin as two potent natural antioxidant, have been used to protect MSCs agianst serum depriviation-induced apoptosis.

Methods: Mesenchymal stem cells were isolated from rats, cultured, then treated with caffeic acid and quercetin with various concentrations at different time. Then they were exposed to serum deprivation for 48 hours. Afterwards, cell survival was assessed using MTT assay and apoptosis was assessed based on the expression of apoptotic and anti-apoptotic proteins including Bax and Bcl-2 using Western blotting.

Results: The results of the present study demonstrated that pretreatment of MSCs with caffeic acid and quercetin after 72-hour significantly increased cell survival in SD conditions. Furthermore, as western blotting has shown that both treatments could decrease Bax protein level and increase Bcl-2 protein expression in SD induced apoptotic cells.

Conclusion: It could be concluded that caffeic acid and quercetin might be used as a promising tools to improve the efficiency of pre-transplant cell therapy.

Keyworde: Caffeic Acid, Quercetin, Bone Marrow Derived Mesenchymal Stem Cells, Apoptosis

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دانشکده داروسازی

پایان نامه خانم مرضیه حیدریان دانشجوی داروسازی ورودی ۹۳ به شماره ۱۲۵۵

تحت عنوان:

بررسی اثر محافظت کنندگی کافئیک اسید و کوئرستین بر آپوپتوز ناشی از محرومیت سرم در سلولهای بنیادی مزانشیمی مشتق از مغز استخوان

استاد (اساتید) راهنما:

دکتر میترا مهربانی

دکتر مهرناز مهربانی

دکتر محمدهادی نعمت الهی

استاد (اساتید) مشاور:

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۱- دکتر فریبا شریفی فر

۲-دکتر صالحه صبوری

در تاریخ **۹۹/۱۱/۰۷** مورد ارزیابی قرار گرفت و با نمره (با عدد) ..۱۹.. (با حروف)..نوزده تام.. به تصویب رسید.

محمدرضا نخعی
کارشناس اداره پایان‌نامه
۹۹/۱۱/۷

دکتر میترا مهربانی
معاون پژوهشی دانشکده

دکتر باقر امیر حیدری
رئیس دانشکده

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